

PATENT COOPERATION TREATY

PCT

NOTICE INFORMING THE APPLICANT OF THE
COMMUNICATION OF THE INTERNATIONAL
APPLICATION TO THE DESIGNATED OFFICES

(PCT Rule 47.1(c), first sentence)

From the INTERNATIONAL BUREAU

To:

DUBUC, Jean, H.
Goudreau Gage Dubuc & Martineau
Walker
The Stock Exchange Tower
Suite 3400, 800 Place Victoria
P.O. Box 242
Montréal, Québec H4Z 1E9
CANADA

Date of mailing (day/month/year)

18 June 1998 (18.06.98)

Applicant's or agent's file reference

CG/10992.14

IMPORTANT NOTICE

International application No.

PCT/CA97/00962

International filing date (day/month/year)

12 December 1997 (12.12.97)

Priority date (day/month/year)

12 December 1996 (12.12.96)

Applicant

INSTITUT DE RECHERCHES CLINIQUES DE MONTREAL et al

1. Notice is hereby given that the International Bureau has communicated, as provided in Article 20, the international application to the following designated Offices on the date indicated above as the date of mailing of this Notice:
- AU, BR, CA, CN, EP, GM, GW, IL, JP, KP, KR, NO, PL, US

In accordance with Rule 47.1(c), third sentence, those Offices will accept the present Notice as conclusive evidence that the communication of the international application has duly taken place on the date of mailing indicated above and no copy of the international application is required to be furnished by the applicant to the designated Office(s).

2. The following designated Offices have waived the requirement for such a communication at this time:

AL, AM, AP, AT, AZ, BA, BB, BG, BY, CH, CU, CZ, DE, DK, EA, EE, ES, FI, GB, GE, GH, HU, ID, IS, KE, KG, KZ,
LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NZ, OA, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR,
TT, UA, UG, UZ, VN, YU, ZW

The communication will be made to those Offices only upon their request. Furthermore, those Offices do not require the applicant to furnish a copy of the international application (Rule 48.1(a-bis)).

3. Enclosed with this Notice is a copy of the international application as published by the International Bureau on 18 June 1998 (18.06.98) under No. WO 98/26063

REMINDER REGARDING CHAPTER II (Article 31(2)(a) and Rule 54.2)

If the applicant wishes to postpone entry into the national phase until 30 months (or later in some Offices) from the priority date, a demand for international preliminary examination must be filed with the competent International Preliminary Examining Authority before the expiration of 18 months from the priority date.

It is the applicant's sole responsibility to monitor the 19-month time limit.

Note that only an applicant who is a national or resident of a PCT Contracting State which is bound by Chapter II has the right to file a demand for international preliminary examination.

REMINDER REGARDING ENTRY INTO THE NATIONAL PHASE (Article 22 or 39(1))

If the applicant wishes to proceed with the international application in the national phase, he must, within 20 months or 30 months, or later in some Offices, perform the acts referred to therein before each designated or elected Office.

For further important information on the time limits and acts to be performed for entering the national phase, see the Annex to Form PCT/IB 301 (Notification of Receipt of Record Copy) and Volume II of the PCT Applicant's Guide.

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No. (41-22) 740.14.35

Authorized officer

J Zahra

Telephone No. (41-22) 338.83.38

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
AM	Armenia	FI	Finland	LT	Lithuania	SK	Slovakia
AT	Austria	FR	France	LU	Luxembourg	SN	Senegal
AU	Australia	GA	Gabon	LV	Latvia	SZ	Swaziland
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BA	Bosnia and Herzegovina	GE	Georgia	MD	Republic of Moldova	TG	Togo
BB	Barbados	GH	Ghana	MG	Madagascar	TJ	Tajikistan
BE	Belgium	GN	Guinea	MK	The former Yugoslav Republic of Macedonia	TM	Turkmenistan
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BY	Belarus	IS	Iceland	MW	Malawi	US	United States of America
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CM	Cameroon		Republic of Korea	PL	Poland		
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DE	Germany	LI	Liechtenstein	SD	Sudan		
DK	Denmark	LK	Sri Lanka	SE	Sweden		
EE	Estonia	LR	Liberia	SG	Singapore		

INTERNATIONAL SEARCH REPORT

Intern Application No
PCT/CA 97/00962

A. CLASSIFICATION OF SUBJECT MATTER IPC 6 C12N15/11 C12N15/12 C07K14/705 G01N33/566 G01N33/50 C12Q1/68 A61K48/00		
According to International Patent Classification (IPC) or to both national classification and IPC		
B. FIELDS SEARCHED Minimum documentation searched (classification system followed by classification symbols) IPC 6 C12N G01N C07K C12Q A61K		
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched		
Electronic data base consulted during the international search (name of data base and, where practical, search terms used)		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	SCHRADER M ET AL: "Thyroid hormone receptor functions as monomeric ligand-induced transcription factor on octameric half-sites: Consequences also for dimerization." JOURNAL OF BIOLOGICAL CHEMISTRY 269 (9). 1994. 6444-6449. ISSN: 0021-9258, XP002061502 see the whole document ---	1-21
Y	PERLMANN T ET AL: "A novel pathway for vitamin A signaling mediated by RXR heterodimerization with NGFI - B and NURR1." GENES & DEVELOPMENT 9 (7). 1995. 769-782. ISSN: 0890-9369, XP002061503 see the whole document ---	1-21
-/--		
<input checked="" type="checkbox"/> Further documents are listed in the continuation of box C. <input checked="" type="checkbox"/> Patent family members are listed in annex.		
* Special categories of cited documents : "A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier document but published on or after the international filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art. "&" document member of the same patent family		
Date of the actual completion of the international search		Date of mailing of the international search report
7 April 1998		23. 04. 1998
Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016		Authorized officer Hix, R

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	GIGUERE V ET AL: "Determinants of Target Gene Specificity for ROR-alpha-1: Monomeric DNA Binding by an Orphan Nuclear Receptor." MOLECULAR AND CELLULAR BIOLOGY 15 (5). 1995. 2517-2526. ISSN: 0270-7306, XP002061504 see table 1	1-21
Y	--- T. E. WILSON ET AL.: "Participation of non-zinc finger residues in DNA binding by two nuclear orphan receptors." SCIENCE, vol. 256, 3 April 1992, pages 107-110, XP002061505 cited in the application see the whole document	1-21
Y	--- PAULSEN R E ET AL: "Three related brain nuclear receptors, NGFI - B, Nurrl, and NOR - 1, as transcriptional activators." JOURNAL OF MOLECULAR NEUROSCIENCE 6 (4). 1995. 249-255. ISSN: 0895-8696, XP002061506 see the whole document	1-21
Y	--- HIRATA Y ET AL: "The phosphorylation and DNA binding of the DNA-binding domain of the orphan nuclear receptor NGFI - B." JOURNAL OF BIOLOGICAL CHEMISTRY 268 (33). 1993. 24808-24812. ISSN: 0021-9258, XP002061507 see the whole document	1-21
X	--- WO 96 21457 A (SALK INST FOR BIOLOGICAL STUDI) 18 July 1996 cited in the application see the whole document	17
Y	--- WILSON, THOMAS E. ET AL: "The orphan receptors NGFI - B and steroidogenic factor 1 establish monomer binding as a third paradigm of nuclear receptor -DNA interaction" MOL. CELL. BIOL. (1993), 13(9), 5794-804 CODEN: MCEBD4;ISSN: 0270-7306, 1993, XP002061508 see the whole document --- -/--	1-21

INTERNATIONAL SEARCH REPORT

Internat Application No
PCT/CA 97/00962

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	T.E. WILSON ET AL.: "Identification of the DNA binding site for NGFI-B by genetic selection in yeast." SCIENCE, vol. 252, 31 May 1991, pages 1296-1300, XP002061509 cited in the application see the whole document ---	1-21
Y	B.M. FORMAN ET AL.: "Unique response pathways are established by allosteric interactions among hormone receptors." CELL, vol. 81, 19 May 1995, pages 541-550, XP002061510 cited in the application see figure 4 ---	1-21
X	E. OATES ET AL.: "5' sequence of Porcine and Rat Pro-opiomelanocortin mRNA." JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 259, no. 12, 25 June 1984, pages 7421-7425, XP002061511 see the whole document ---	5,6
X	M. THERRIEN ET AL.: "Pituitary Pro-opiomelanocortin gene expression requires synergistic interactions of several regulatory elements." MOLECULAR AND CELLULAR BIOLOGY, vol. 11, no. 7, July 1991, pages 3492-3503, XP000570346 see the whole document ---	5,6
X	J. DROUIN ET AL.: "Structure of the rat pro-opiomelanocortin {POMC} gene." FEBS LETTERS, vol. 193, no. 1, November 1985, pages 54-58, XP002061512 see the whole document ---	5,6
Y,P	A. PHILIPS ET AL.: "Antagonism between Nur77 and Glucocorticoid receptor for control of transcription." MOLECULAR AND CELLULAR BIOLOGY, vol. 17, no. 10, October 1997, pages 5952-5959, XP002061513 see the whole document ---	1-21
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INTERNATIONAL SEARCH REPORT

Intern Application No
PCT/CA 97/00962

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X,P	<p>A. PHILIPS ET AL.: "Novel dimeric Nur77 signalling mechanism in endocrine and lymphoid cells." MOLECULAR AND CELLULAR BIOLOGY, vol. 17, no. 10, October 1997, pages 5946-5951, XP002061514 see figure 6B</p> <p>-----</p>	1-21

INTERNATIONAL SEARCH REPORT

application No.

PCT/CA 97/ 00962

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
Remark: Although claim(s) 21
is(are) directed to a method of treatment of the human/animal
body, the search has been carried out and based on the alleged
effects of the compound/composition.
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such
an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all
searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment
of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report
covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is
restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

Internal Application No

PCT/CA 97/00962

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9621457 A	18-07-96	AU 4530496 A CA 2210248 A EP 0809509 A	31-07-96 18-07-96 03-12-97

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference CG/10992.14	FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. PCT/CA 97/ 00962	International filing date (day/month/year) 12/12/1997	(Earliest) Priority Date (day/month/year) 12/12/1996
Applicant INSTITUT DE RECHERCHES CLINIQUES DE ... et al.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 6 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. ☒ Certain claims were found unsearchable (see Box I).

2. ☐ Unity of invention is lacking (see Box II).

3. ☒ The international application contains disclosure of a nucleotide and/or amino acid sequence listing and the international search was carried out on the basis of the sequence listing

☐ filed with the international application.

☒ furnished by the applicant separately from the international application,

☐ but not accompanied by a statement to the effect that it did not include matter going beyond the disclosure in the international application as filed.

☐ Transcribed by this Authority

4. With regard to the title, ☒ the text is approved as submitted by the applicant.

☐ the text has been established by this Authority to read as follows:

5. With regard to the abstract,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this International Search Report, submit comments to this Authority.

6. The figure of the drawings to be published with the abstract is:

Figure No. 3D

☒ as suggested by the applicant.

☐ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

☐ None of the figures.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/CA 97/00962

Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
Remark: Although claim(s) 21 is(are) directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.

☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/ 97/00962

A. CLASSIFICATION OF SUBJECT MATTER

IPC 6 C12N15/11 C12N15/12 C07K14/705 G01N33/566 G01N33/50
C12Q1/68 A61K48/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 C12N G01N C07K C12Q A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	SCHRADER M ET AL: "Thyroid hormone receptor functions as monomeric ligand-induced transcription factor on octameric half-sites: Consequences also for dimerization." JOURNAL OF BIOLOGICAL CHEMISTRY 269 (9). 1994. 6444-6449. ISSN: 0021-9258, XP002061502 see the whole document ---	1-21
Y	PERLMANN T ET AL: "A novel pathway for vitamin A signaling mediated by RXR heterodimerization with NGFI - B and NURR1." GENES & DEVELOPMENT 9 (7). 1995. 769-782. ISSN: 0890-9369, XP002061503 see the whole document --- -/--	1-21

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

° Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *Z* document member of the same patent family

Date of the actual completion of the international search

7 April 1998

Date of mailing of the international search report

23. 04. 1998

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Hix, R

INTERNATIONAL SEARCH REPORT

International Application No

PCT/97/00962

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		Relevant to claim No.
Category *	Citation of document, with indication, where appropriate, of the relevant passages	
Y	GIGUERE V ET AL: "Determinants of Target Gene Specificity for ROR-alpha-1: Monomeric DNA Binding by an Orphan Nuclear Receptor." MOLECULAR AND CELLULAR BIOLOGY 15 (5). 1995. 2517-2526. ISSN: 0270-7306, XP002061504 see table 1	1-21
Y	--- T. E. WILSON ET AL.: "Participation of non-zinc finger residues in DNA binding by two nuclear orphan receptors." SCIENCE, vol. 256, 3 April 1992, pages 107-110, XP002061505 cited in the application see the whole document	1-21
Y	--- PAULSEN R E ET AL: "Three related brain nuclear receptors, NGFI - B, Nurrl, and NOR - 1, as transcriptional activators." JOURNAL OF MOLECULAR NEUROSCIENCE 6 (4). 1995. 249-255. ISSN: 0895-8696, XP002061506 see the whole document	1-21
Y	--- HIRATA Y ET AL: "The phosphorylation and DNA binding of the DNA-binding domain of the orphan nuclear receptor NGFI - B." JOURNAL OF BIOLOGICAL CHEMISTRY 268 (33). 1993. 24808-24812. ISSN: 0021-9258, XP002061507 see the whole document	1-21
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Y	--- WILSON, THOMAS E. ET AL: "The orphan receptors NGFI - B and steroidogenic factor 1 establish monomer binding as a third paradigm of nuclear receptor -DNA interaction" MOL. CELL. BIOL. (1993), 13(9), 5794-804 CODEN: MCEBD4;ISSN: 0270-7306, 1993, XP002061508 see the whole document	1-21
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INTERNATIONAL SEARCH REPORT

International Application No
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Y	--- B.M. FORMAN ET AL.: "Unique response pathways are established by allosteric interactions among hormone receptors." CELL, vol. 81, 19 May 1995, pages 541-550, XP002061510 cited in the application see figure 4	1-21
X	--- E. OATES ET AL.: "5' sequence of Porcine and Rat Pro-opiomelanocortin mRNA." JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 259, no. 12, 25 June 1984, pages 7421-7425, XP002061511 see the whole document	5,6
X	--- M. THERRIEN ET AL.: "Pituitary Pro-opiomelanocortin gene expression requires synergistic interactions of several regulatory elements." MOLECULAR AND CELLULAR BIOLOGY, vol. 11, no. 7, July 1991, pages 3492-3503, XP000570346 see the whole document	5,6
X	--- J. DROUIN ET AL.: "Structure of the rat pro-opiomelanocortin {POMC} gene." FEBS LETTERS, vol. 193, no. 1, November 1985, pages 54-58, XP002061512 see the whole document	5,6
Y,P	--- A. PHILIPS ET AL.: "Antagonism between Nur77 and Glucocorticoid receptor for control of transcription." MOLECULAR AND CELLULAR BIOLOGY, vol. 17, no. 10, October 1997, pages 5952-5959, XP002061513 see the whole document --- -/--	1-21

INTERNATIONAL SEARCH REPORT

International Application No
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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

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INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/97/00962

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9621457 A	18-07-96	AU 4530496 A	31-07-96
		CA 2210248 A	18-07-96
		EP 0809509 A	03-12-97
